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AUTHOR Mulroy, Kevin
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ABSTRACT

Clozapine is an antipsychotic medication used in the treatment of schizophrenia. This paper reviews articles concerning clozapine therapy. It considers its benefits and dangers in various situations, and how it can be successfully combined with talk therapies. Studies are reviewed concerning patients in outpatient clinics, partial hospitalization programs, and full hospitalization programs. The reviews conclude that neither drug therapy nor talk therapy alone is sufficient. The collusion of patient, doctor, and family is necessary if a successful resolution of the patient's problem is to be obtained. (JDM)

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Combining Clozapine and Talk Therapies

Kevin Mulroy

Department of Education, Guam

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K Mulroy

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Abstract

This paper is a review of articles concerning clozapine therapy, its benefits and its dangers, in various situations; and, how it is profitably combined with talk therapies. We will look at studies done in outpatient clinics, partial hospitalization programs, and full hospitalization programs. We shall see the varying effects on patient and family. The conclusion being that neither drug therapy alone nor talk therapy alone is sufficient. It is further seen that the collusion of patient, doctor, and family must also be added to the mix if a successful resolution of the patient s problem is to be brought about.

Combining Clozapine and Talk Therapies

Clozapine is an antipsychotic medication used in the treatment of schizophrenia. It can have a powerful effect on both positive symptoms (such as, delusions and hallucinations), and negative symptoms (such as depression). We shall see how this medication is related to the prevention of suicide on the one hand, and to the causation of death on the other hand if not properly monitored.

Since this medication is so effective in its results, and is administered by medically trained personnel who may not have an awareness of the value of adding talk therapy to the treatment, it often becomes the sole method of attacking the disorder. Research tends to be limited to the various settings and methods by which the drug might be delivered.

As a result of the higher levels of functioning produced by the drug therapy, both patients and their families have a need to cope with the new demands of social functioning. Unless these demands are successfully met by the affected individuals, it is likely that relapse may occur. For this reason, talk therapies are more often combined with the drug therapy, and we are seeing more studies of this nature.

The consensus of medical personnel and other therapists seems to predominantly favor a joint approach. It is interesting to see researchers attempt to specify what types of patients, in what settings, with what specific talk therapy, and in what stage of development are most benefited. This will certainly lead to a maximization of effect.

As stated, clozapine is a very powerful medication. On the one hand, it is powerful enough to cause death, while on the other hand, it can be effective in the prevention of suicide. Normally, suicides occur at the rate of 10-15% in schizophrenic and schizoaffective

patients. However, the proper use of clozapine can reduce this risk to normal levels. (Reid, Mason and Hogan, 1998).

The mental states of these patients are affected by coincidental major depression. During times that they are lucid, they realize that they have a severe disorder that is limiting every area of their life. Delusions and hallucinations are among those limiting and destructive factors. Medication related factors include severe side effects such as Tardive Dyskinesia. The depression that results may cause notions that suicide is a rational decision. (Reid et al. 1998).

Clozapine helps because it reduces not only the positive symptoms of the disease, but also the negative symptoms. There was found an 86% reduction in suicidal thoughts and actual suicides in one study and an 82% reduction in suicide in another study. (Reid et al. 1998).

In the Texas public mental health system, where the drug was first used, the annual suicide rate for schizophrenic and schizoaffective patients was 60.2 per 100,000. This compared with a general population rate of 12.0 and a 12.4 rate for clozapine patients. There were more females in this group than in the general schizophrenic and schizoaffective populations; however, there are no significant differences in the suicide rate in the general population for males vs females so this was not considered a confounding issue. No confounding issues were found at all. Indeed, it is noted that the patients selected were the most severely disturbed, and at higher risk than those not selected. (Reid et al. 1998).

Patients were more likely to follow their drug protocol because they had to receive their medication from a physician at a weekly appointment to monitor their white blood

cell count. The conclusion offered by the authors is that the proper usage and delivery of clozapine will be instrumental in a lower suicide rate. Talk therapies were not a part of this study. (Reid et al. 1998).

For all the benefits that clozapine offers, it remains a dangerous drug. White blood cell suppression must be monitored weekly or it could advance to the point of death. A national registry of clozapine patients was established. It has two purposes. The first was to monitor the progress of patients in treatment so as to prevent agranulocytosis. The second purpose is to prevent the retreatment of patients who had already demonstrated agranulocytosis. (Honingfeld, 1996).

Medication is given weekly through physicians who are part of the national registry. If these physicians fail to report adequately on their patients, they can be removed from the system. All data received are entered into a computerized system maintained by the manufacturer. This data is reported weekly. Two areas were investigated by the author: adherence to agency protocols and denial of treatment. These were compared to rates of agranulocytosis and deaths related to agranulocytosis. (Honingfeld, 1996).

With regard to adherence to agency protocol, Honingfeld found that over 97% of participating physicians were complying adequately. With regard to denial of retreatment, the number of patients attempting this was small, and retreatment was appropriately denied. In some cases, the manufacturer was given identification numbers for a group of non-retreatable patients as a test, and the false patients were correctly denied retreatment. (Honingfeld, 1996).

Given the excellent monitoring of the drug s delivery, one would expect that rates of death associated with agranulocytosis would be low. Among a total of 99,502 followed,

there was a rate of agranulocytosis of 0.38%. The rate of associated death was 0.012%. Premarket clinical research predicted an associated death incidence of 149 persons, but the actual incidence was only 12 persons. (Honingfeld, 1996).

Clozapine has been delivered in outpatient programs, in partial hospitalization programs, and in full hospitalization programs. The choice appears to be mainly based on the severity of the patient s disorder.

Outpatient Programs

A study of moderately ill schizophrenic patients indicates that the relapse rates under clozapine, as opposed to the year before with older drugs, showed significant improvements. This was especially true of the positive symptoms. Negative symptoms also seemed to improve, but not significantly. Four months seemed to be the time period in which responses to the medication could be identified. (Breier, Buchanan, Irish, and Carpenter, 1993).

The study used a 10-week double blind experiment; and, then entered into a one year long descriptive phase. 60% of those patients finishing the study showed sustained clinical improvement. Relapses and hospitalizations were significantly reduced. These patients matched characteristics found in the general population of clinical outpatients. Only one exception was made in that substance abusers were excluded. (Breier et al. 1993).

Other studies report significant improvement in negative symptoms. The differences from the previous study may be attributable to differences in patient populations and the intensity of the disorder in individuals. The wider use of clozapine may then have major clinical and public health impact on the care of schizophrenic patients . (Breier et al. 1993).

Partial Hospitalization Programs

Many clinicians are reluctant to begin clozapine therapy without hospitalization of the client particularly in the case of individuals with severe disorders. The hospitalization, however, may only be short-term. For example, this particular program starts the therapy in the hospital and titrates the patient there. Then, the patient can be released and followed up in the community clinic. In the early stages, the patient is not only carefully monitored until responding, but also escapes the probable increased social demands (including familial obligations) that come with improvement. This is referred to as a paradoxical effect, as it is contrary to expectations. The study was done at the Schizophrenia Research Treatment and Rehabilitation Center in Decatur, Georgia. It was a structured format that combined individual and group therapy, nursing services, rehabilitative services, supervised community-based housing, training in vocational and living skills, on-site psychiatric services, patient and family education, and 24 hour emergency services. (Johnson, Littrell, and Magill (1994).

To insure compliance, clozapine was initially administered by staff only. Later, some patients were given responsibility for administering their own medication. Patients' white blood cell counts were taken weekly. In addition, staff were trained to look for early signs of agranulocytosis (mainly, flu-like symptoms). (Johnson et al. 1994).

Tardive Dyskinesia movements were cut in half soon after the titration period was over. Psychiatric symptoms, positive and negative, were greatly reduced; and, rehospitalizations were reduced significantly. Social functioning continued to improve during the 12 months of the study. 44 of 47 patients reported working at paid or volunteer

jobs. The study suggests that this form of delivery can be effective for certain patients. (Johnson et al. 1994).

Full Hospitalization Programs

For severely disordered patients who were also treatment resistant to the older antipsychotic medications, there is little choice. In one study, after treating 37 such patients for 6 months, 34 of them still remained in hospital. However, their social functioning within the hospital setting improved a great deal. The social functioning was measured in several ways, such as violent episodes, assaults, self-harm, etc. (Wilson, 1992).

All of these patients had been treated with older antipsychotic medications before being treated with clozapine. Minor side effects such as tachycardia and hypersalivation occurred. No patients quit the program. Dyskinesia decreased as did positive and negative symptoms. However, the number of patients in the study was small and this might have confounded the results obtained. (Wilson, 1992).

Violent episodes immediately began to decrease from a monthly high of 70 episodes to an incidence rate of 10 per month. This is far lower than the lowest pre-clozapine rate of 30 per month. The number of patients involved in violent episodes in any given month reached a high of 18 in the pre-clozapine period. During clozapine therapy, it decreased to 8 per month. Throughout the six months patients continued to move from the unimproved category to improved to much improved. (Wilson, 1992).

Clozapine generally worked well. Only 3 patients were discharged, but this was to be expected with the severely disturbed group that was used for the study. Agranulocytosis

did not occur. This was also to be expected given the small size of the group. The signs of social functioning were there, and the improvement in this area kept rising beyond the six month level. Seizures were more evidenced than expected, but this could have been a statistical fluke. (Wilson, 1992).

In another study of full hospitalization, it was explained that many patients receive this medication through the public health system of their state because of the cost of the drug and the need to monitor its delivery. The public sector total was45% in 1991 and each state had plans to increase that percentage. The successes of clozapine were becoming widely known. Since an enormous amount of money is spent on schizophrenia and schizoaffective disorders, this drug seemed to hold the key for reduced spending as well as an increased quality of life for the affected clients. (Reid, Pham, and Rago, 1993).

Clozapine helps some of the more severely disturbed mental patients. Many of them could not be helped in any way without clozapine. While it is an expensive drug, it also has the effect of reducing the other costs associated with the disorders such as hospitalization and eventual total disability. Here is a safe, effective medication that will cure a terribly debilitating disorder and be cost-effective over the long run. (Reid et al. 1993).

Patients and Families

The use of this powerful drug can bring about dramatic changes in the patient. However, these changes can cause expectations in the patient and family that are unrealistic. These expectations can lead to breakdown of the clozapine trial with a given individual. In the pretreatment phase, patients and families are optimistic that clozapine will bring this debilitating disorder under control. This is good. It means that families will

enthusiastically assist the effort to help the patient. Family members, however, may be too hopeful that the patient (who may not have demonstrated much compliance in the past) will be able to work fully with the trial. They may even be intimidating to the patient. Like certain medical personnel, and even because of them, the family may feel that clozapine will do everything that is necessary to be done. As a result, they may be indifferent, or even hostile, to the addition of talk therapies. Preexisting problems in the family structure will probably be intensified at this time. Various family members may work in opposition instead of cooperation. A family therapist needs to work with them at this time to bring about the necessary process of cooperating for realistic goals. (Kotcher and Smith, 1993).

Once treatment begins, the discrepancies between reality and expectation take tangible form. Moving a patient from other antipsychotics to clozapine often involves a period when the various symptoms of the disorder temporarily return. This is, of course, very upsetting to patient and family even though they know it is coming. At this stage, the patient may decide that the side effects, return of symptoms, and weekly monitoring of white blood cells is just too much to handle for the sake of some new (to the patient) drug therapy that has not yet kicked in. This leads to further anxieties between family and patient. Therapists should utilize a variety of treatments at this point, such as psychoeducation, stress relief, and multifamily groups. (Kotcher and Smith, 1993).

In the later stages of the trial, three to nine months after clozapine has been started, some anxieties remain. Families have either come closer together, or moved further apart. depending on the success of the drug. Success leads to new demands on the social functioning of both patient and family. These demands can cause breakdown. On the other hand, lack of improvement can cause complete demoralization. Treatment in successful

trials focuses on coping strategies for the new demands of life. A deep psychodynamic therapy, such as object relations therapy, is necessary at this point to integrate the family structure by understanding the splits and failures that have occurred. (Kotcher and Smith, 1993).

A long-term study evaluated cognitive functioning, dyskinetic movements, and discharge rates. Reductions in symptoms were observed and the majority of patients were able to be discharged. Clozapine, when combined with psychosocial treatment, is effective for treatment of patients with schizophrenia who are not responsive to other medications . (Grace et al. 1996).

None of 31 patients were dismissed during the first two years of the study. 22 patients completed the three years of the study. The combined therapies had a clear effect on the patients. Patients appeared to be not only improved in their positive and negative symptoms, but also in their cognitive functioning as observed on various measures. Only two of the discharged patients required rehospitalization. (Grace et al. 1996).

The final study discusses the effects of clozapine and social learning in severely disturbed psychiatric patients in a state hospital situation. The conclusion of the authors was that clozapine produced the necessary improvement in positive and negative symptoms for social learning to happen resulting in cognitive and emotional changes for long-term behavioral change. (Menditto et al., 1996).

One of the interesting products of this study was a focus on aggressive behaviors, Aggressive did seem to have been reduced by the combined therapies. A great number of patients were discharged from this program. It used a token economy system which

allowed for operant conditioning learning of the social and self-help skills needed by the patients. Baseline measurements were taken before the start of the program. The 22 patients in the study were initially receiving dosages of older antipsychotics. (Menditto et al. 1996).

The data from the study suggest that social learning appears to be a powerful additive to drug therapy alone. The reverse is also true. That clozapine is a powerful additive to talk therapy. a large proportion of the main effects found in this study appear to have occurred as a response to the social learning program before the introduction of clozapine. Nevertheless, the data suggest that the addition of clozapine resulted in greater improvements for a select group of patients . (Menditto et al. 1996).

It is not sufficient to do drug therapy alone. One sees that the patient, medical personnel, talk therapists, and family must all be in collusion if a satisfactory resolution is to be brought about. (Kotcher and Smith, 1993).

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